William !

9 /48587**9**

93

PCT/EP98/05360

416 Rec'd PCT/PTO 1 6 FEB 2000

PATENT CLAIMS

- 1. Method for the multiple characterization of disseminated and micrometastasized cancer cells on the basis of DNA and/or RNA, wherein cells obtained from body fluid from an individual are investigated for at least one cancer-specific gene on the basis of mRNA; and cancer cells removed from body fluid from an individual are investigated for at least one cancer-specific gene on the basis of DNA and/or mRNA.
- 2. Method according to Claim 1, characterized in that expression analyses on the basis of mRNA are carried out on those cancerspecific genes which are essentially not expressed in non-cancer cells in the body fluid investigated.
- 3. Method according to Claim 2, characterized in that mRNA of the CEA, CK20, MUC1, tyrosinase and/or MAGE3 genes is investigated.
- 4. Method according to Claim 1, characterized in that genomic DNA of the p53, erb-B2, c-myc, K-ras, RB, APC and/or DCC genes is investigated.
- 5. Method according to any of the preceding claims, characterized in that genomic DNA is investigated for mutations, amplifications, LOHs, translocations and/or polymorphisms of oncogenes and/or mutated tumour suppressor genes.
- 6. Method according to any of the preceding claims, characterized in that the cells and/or the cancer cells are additionally investigated for at least one cancer-associated gene.

- 7. Method according to Claim 6, characterized in that investigation is for tissue-specific genes, metastasis-associated genes, steroid hormone receptor genes, drug resistance genes and/or genes which correlate with immunomodulation, cell proliferation and/or apoptosis.
- 8. Method according to Claim 7, characterized in that investigation is for metastasis-associated genes which code for angiogenesis factors, motility factors, growth factors, matrix degradation factors such as proteinases and their inhibitors, and/or adhesion factors such as adherins.
- 9. Method according to any of Claims 6 to 8, characterized in that mRNA is investigated.
- 10. Method according to Claim 9, characterized in that mRNA of the bFGF, bFGF-R, VEGF, VEGF-R1, VEGF-R2, MMP2 and/or TIMP3 genes is investigated.
- 11. Method according to any of the preceding claims, characterized in that cancer cells are removed from the body fluid or from cell-containing fractions thereof by immunoadsorption, microfiltration or density gradient centrifugation.
- 12. Method according to Claim 11, characterized in that single cancer cells are removed and are also investigated singly.
- 13. Method according to any of the preceding claims, characterized in that an investigation established with cancer cells is also carried out with non-cancer cells from the same individual for comparison.
- 14. Use of the method according to any of Claims 1 to 13 for the in vitro diagnosis of cancer.

- 15. Use of disseminated and micrometastasized cancer cells characterized by the method according to any of Claims 1 to 13 for testing active substances for an antineoplastic effect.
- 16. Means for carrying out the method according to any of Claims 1 to 13, comprising suitable primers, probes and/or positive/negative controls and, where appropriate, other means usual for the characterization of DNA and/or RNA.
- 17. Means according to Claim 16 in the form of a combination of test kits and/or diagnostic kits.

AND CE